Percutaneous coronary intervention or coronary artery bypass graft in left main coronary artery disease: a comprehensive meta-analysis of adjusted observational studies and randomized controlled trials

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Abstract: BACKGROUND Treatment of patients with ULMCA (unprotected left main coronary artery disease) with percutaneous coronary intervention (PCI) has been compared with coronary artery bypass graft (CABG), without conclusive results. METHODS All randomized controlled trials (RCTs) and observational studies with multivariate analysis comparing PCI and CABG for ULMCA were included. Major cardiovascular events (MACEs, composite of all-cause death, MI, definite or probable ST, target vessel revascularization and stroke) were the primary end points, whereas its single components were the secondary ones, along with stent thrombosis, graft occlusion and in-hospital death and stroke. Subgroup analyses were performed according to Syntax score. RESULTS Six RCTs (4717 patients) and 20 observational studies with multivariate adjustment (14 597 patients) were included. After 5 (3-5.5) years, MACE rate was higher for PCI [odds ratio (OR) 1.10, 95% confidence interval (CI) 1.07-1.14], without difference in death, whereas more relevant risk of MI was because of observational studies. Coronary stenting increased risk of revascularization (OR 1.52; 95% CI 1.34-1.72). At meta-regression, performance of PCI was improved by use of intra-coronary imaging and worsened by first generation stents, whereas two arterial grafts increased benefit of CABG. For patients with Syntax score less than 22, MACE rates did not differ, whereas for higher values, CABG reduced MACE because of lower risk of revascularization. Incidence of graft occlusion was 3.24% (2.25-4.23), whereas 2.13% (1.28-2.98: all CI 95%) of patients experienced stent thrombosis. CONCLUSION Surgical revascularization reduces risk of revascularization for ULMCA patients, especially for those with Syntax score greater than 22, with a higher risk of in-hospital death. Intra-coronary imaging and use of arterial grafts improved performance of revascularization strategies.

DOI: https://doi.org/10.2459/JCM.0000000000000703

FIC Federazione Italiana di Cardiologia
Italian Federation of Cardiology

Percutaneous coronary intervention or coronary artery bypass graft in left main coronary artery disease: a comprehensive meta-analysis of adjusted observational studies and randomized controlled trials

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Background **Treatment of patients with ULMCA (unprotected left main coronary artery disease) with percutaneous coronary intervention (PCI) has been compared with coronary artery bypass graft (CABG), without conclusive results.**

Methods **All randomized controlled trials (RCTs) and observational studies with multivariate analysis comparing PCI and CABG for ULMCA were included. Major cardiovascular events (MACEs, composite of all-cause death, MI, definite or probable ST, target vessel revascularization and stroke) were the primary end points, whereas its single components were the secondary ones, along with stent thrombosis, graft occlusion and in-hospital death and stroke. Subgroup analyses were performed according to Syntax score.**

Results **Six RCTs (4717 patients) and 20 observational studies with multivariate adjustment (14 597 patients) were included. After 5 (3–5.5) years, MACE rate was higher for PCI [odds ratio (OR) 1.10, 95% confidence interval (CI) 1.07–1.14], without difference in death, whereas more relevant risk of MI was because of observational studies. Coronary stenting increased risk of revascularization (OR 1.52; 95% CI 1.34–1.72). At meta-regression, performance of PCI was improved by use of intra-coronary imaging and worsened by first generation stents, whereas two arterial grafts increased benefit of CABG. For patients with Syntax score less than 22, MACE rates did not differ, whereas for higher values, CABG reduced MACE because of lower risk of revascularization. Incidence of graft occlusion was 3.24% (2.25–4.23), whereas 2.13% (1.28–2.98: all CI 95%) of patients experienced stent thrombosis.**

Conclusion **Surgical revascularization reduces risk of revascularization for ULMCA patients, especially for those with Syntax score greater than 22, with a higher risk of in-hospital death. Intra-coronary imaging and use of arterial grafts improved performance of revascularization strategies.**

J Cardiovasc Med 2018, **19**:554–563

Keywords: coronary artery bypass graft, coronary artery disease, left main, percutaneous coronary intervention, surgery, left main percutaneous

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Received 13 January 2018 **Revised** 4 April 2018
Accepted 21 July 2018

Introduction

The high risk related to stenosis of unprotected left main coronary artery (ULMCA) and its negative prognostic impact is largely known. This condition is reported in about 6% of patients undergoing coronary angiography both for acute coronary syndromes as in stable angina.[1] Coronary artery bypass grafting (CABG) has long been considered the treatment of choice for ULMCA.[2] Development of drug-eluting stents (DESs) and use of imaging

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DOI:10.2459/JCM.0000000000000703

techniques increased use of percutaneous coronary intervention (PCI) with satisfactory results even at long-term follow-up.[3,4] Some randomized controlled trials (RCTs) compared PCI and CABG demonstrating similar results in terms of death, myocardial infarction (MI) and stroke with a benefit of CABG in terms of lower subsequent revascularization.[5,6] Use of multiple arterial grafts and of new generation DESs has been advocated by cardiac surgeons and interventional cardiologists, respectively, as a promising strategy in this field, but contrasting data have been recently provided.[7,8] A recent meta-analysis based only on RCTs and including last published articles with newest DESs generation confirmed similar efficacy between the two approaches except for higher repeated revascularization with PCI.[9] Data from observational studies with multivariate adjustment may be of interest, in order to increase the body of evidence expanding the sample size from one side, and to test the reproducibility of RCTs results to real life patients, often excluded from RCTs.[10]

The aim of this meta-analysis is to overcome the lack of clear scientific evidence by pooling data from available RCTs, propensity-score-adjusted trials and studies performing Cox multivariate analysis.

Methods

The present study was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses statements (PRISMA).[11–15] PubMed, Cochrane, and Google Scholar were searched for the following terms: 'coronary artery bypass' and 'coronary stenting' and 'multivessels disease' and 'left main disease' by two authors (M.B. and O.D.F.). Citations were first screened independently by two reviewers (M.I. and F.D.A.), with disagreements resolved by consensus. Inclusion criteria were human studies, comparing PCI with CABG for left main revascularization, with a follow-up longer than 3 years and more than 50 included patients to avoid limited sample effect. In the case of duplicate reporting, the manuscript with the largest sample of patients was selected. By authors' choice, articles not written in English were excluded from this analysis.

Data abstraction

The following data were independently abstracted by two reviewers (M.I. and F.D.A.) on prespecified electronic forms, with disagreements resolved by consensus: authors, journal, year of publication, location of the study group, type of DES, baseline, angiographic and procedural features, kind of bypass graft and definition of bleeding were collected. The corresponding authors of the relevant studies were queried to provide quantitative details not available in the published manuscripts and were included in the project (see appendix, web only, http://links.lww.com/JCM/A134).

End points

Major cardiovascular events [MACEs: composite of all-cause death, MI, definite or probable ST, target vessel revascularization (TVR)] was the primary end point, whereas its single components were the secondary ones, along with graft occlusion, target lesion revascularization (TLR) and in-hospital death and stroke. Subgroup analyses for MACEs, death and revascularization were performed according to Syntax score. Meta-regression analysis was performed to evaluate impact of site of stenosis and of choice of strategies on revascularization.

Quality study evaluation

The quality of included studies was independently appraised by two reviewers (M.I. and F.D.A.), with disagreements resolved by consensus. For each RCT, we evaluated the risk of bias (low, moderate, unclear, or high) for random-sequence generation, allocation concealment, blinding of patients and physicians, blinding during assessment of follow-up, incomplete outcome evaluation, and selective reporting, in keeping with the Cochrane Collaboration approach (see appendix, table S1-S2, web only, http://links.lww.com/JCM/A134).

Statistical analysis

Continuous variables are reported as mean (SD) or median (first and third quartile). Categorical variables are expressed as *n* (%). Statistical pooling for incidence estimates was performed according to a random-effect model with generic inverse-variance weighting, computing risk estimates with 95% confidence intervals (CIs), using RevMan 5.2 (The Cochrane Collaboration, The Nordic Cochrane Centre, Copenhagen, Denmark). Small study bias was appraised by graphical inspection of funnel plots. Meta-regression analysis was performed to assess the impact of baseline features on the primary end point with comprehensive meta-analysis software (trial version). Hypothesis testing for superiority was set at the two-tailed 0.05 level. Hypothesis testing for statistical homogeneity was set at the two-tailed 0.10 level and based on the Cochran Q test, with I2 values of 25, 50, and 75% representing mild, moderate, and severe heterogeneity, respectively.

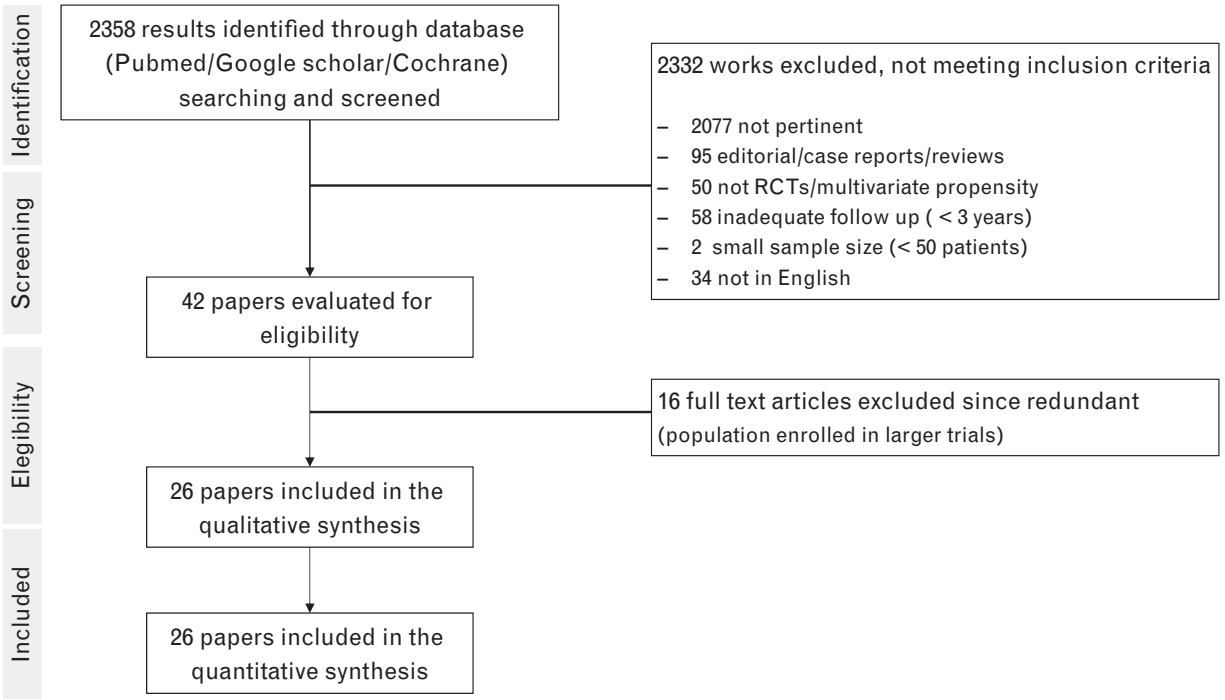
Statistical methods and baseline and interventional variables included in the propensity score matching/multivariate analysis of observational studies are described in appendix table S6 A-B (web only), http://links.lww.com/JCM/A134.

Results

Studies selection and baseline features

A total of 2358 results emerged from the key research used. After an accurate analysis of title, abstract and, if necessary, full-text, 2332 works were excluded as they did not full-fill inclusion criteria previously stated. In particular, 2077 were ruled out as not pertinent, 34 were

Fig. 1



Study design and review's profile. Twenty-six articles were finally selected for the systematic review and meta-analysis, 6 randomized controlled trials (RCTs) and 20 observational studies with multivariate adjustment or propensity score analysis (NRCTs) with a total of 19 314 patients included in the analysis, of which 8501 treated with PCI and 10 813 with CABG. PCI, percutaneous coronary intervention.

not in English, 95 results were editorials/case report/reviews, 50 were neither RCTs nor multivariate adjusted studies, 58 had an inadequate follow-up (<3 years) and 2 studies were excluded because of a small sample size (<50 patients). Of 42 results first selected, 16 were then judged as redundant as conducted among a population enrolled in a larger trial. Twenty-six articles were finally selected for the systematic review and meta-analysis: 6 RCTs and 20 observational studies with multivariate adjustment or propensity score analysis (NRCTs) (see appendix, web only, http://links.lww.com/JCM/A134). Nineteen thousand three hundred and fourteen patients were included in the final analysis, of which 8501 were treated with PCI and 10813 with CABG. Four thousand seven hundred and seventeen patients were enrolled in RCTs (2360 in PCI group and 2357 in CABG group) and 14597 in NRCTs (6141 in PCI group and 8456 in CABG group, see Fig. 1).

Mean age of overall population was 64 ± 9 years; 26% were women, 64% were hypertensive patients, and 32% were diabetic. Median Syntax score was 26, whereas single-study Euroscore value and type are described in Table S4A (web appendix only, http://links.lww.com/JCM/A134); 12% of the patients had a single lesion of left main, whereas distal left main stenosis was reported in 65% of them (see Tables 1 and 2 for overall data and Table S4-S5, web appendix only, for specific single-study data, http://links.lww.com/JCM/A134).

Primary endpoint analysis

Twenty-two of the 26 included studies (6 RCTs including 4717 patients and 16 NRCTs for 13 375 patients)

Table 1 Baseline features of included patients

	Total population, $n = 19\,314$ (PCI 8501, CABG 10813)
Age (years)	64 ± 9
Female (%)	26 (21–29)
Diabetes (%)	32 (26–39)
Hypertension (%)	64 (58–68)
Hyperlipidemia (%)	54 (51–70)
BMI	26 ± 2
Family history of CAD (%)	17 ± 8 (9–19)
Current smokers (%)	35 (20–48)
Previous AMI (%)	22 (7–41)
EF	55 ± 6
Previous PCI (%)	16 (9–29)
Previous stroke (%)	9 (2–13)
BPCO (%)	5 (1–7)
Periferal vascular disease (%)	10 (2–17)
IRC (%)	8
Syntax score	26 ± 5
Clinical presentation	
STEMI	2.2 ± 4%
NSTEMI	12 ± 16%
UA	46 ± 18%
Stable angina	37 ± 17%
Silent ischemia	2.8 ± 2

AMI, acute myocardial infarction; BMI, body mass index; BPCO, chronic obstructive pulmonary disease; CABG, coronary artery bypass graft; CAD, coronary artery disease; EF, ejection fraction; IRC, chronic renal insufficiency; NSTEMI, non ST elevation myocardial infarction; PCI, percutaneosu coronary intervention; STEMI, ST elevation myocardial infarction; UA, unstable angina.

Table 2 Interventional features of included patients

Procedural features	Total population, $n = 19\,314$ (PCI 8501, CABG 10813)
Distal left main	65 (54–74)
Only left main	12 (2–21)
First generation DES/BMS	83 (80–84)
Use of IVUS	63 (40–81)
Final kissing balloon	46 (30–51)
On pump surgery	64 (45–71)
Two arterial grafts	50 (16–64)
Complete revascularization	84 (78–82)

BMS, bare metal stents; CABG, coronary artery bypass graft; DES, drug eluting stents; IVUS, intravascular ultrasound; PCI, percutaneous coronary intervention.

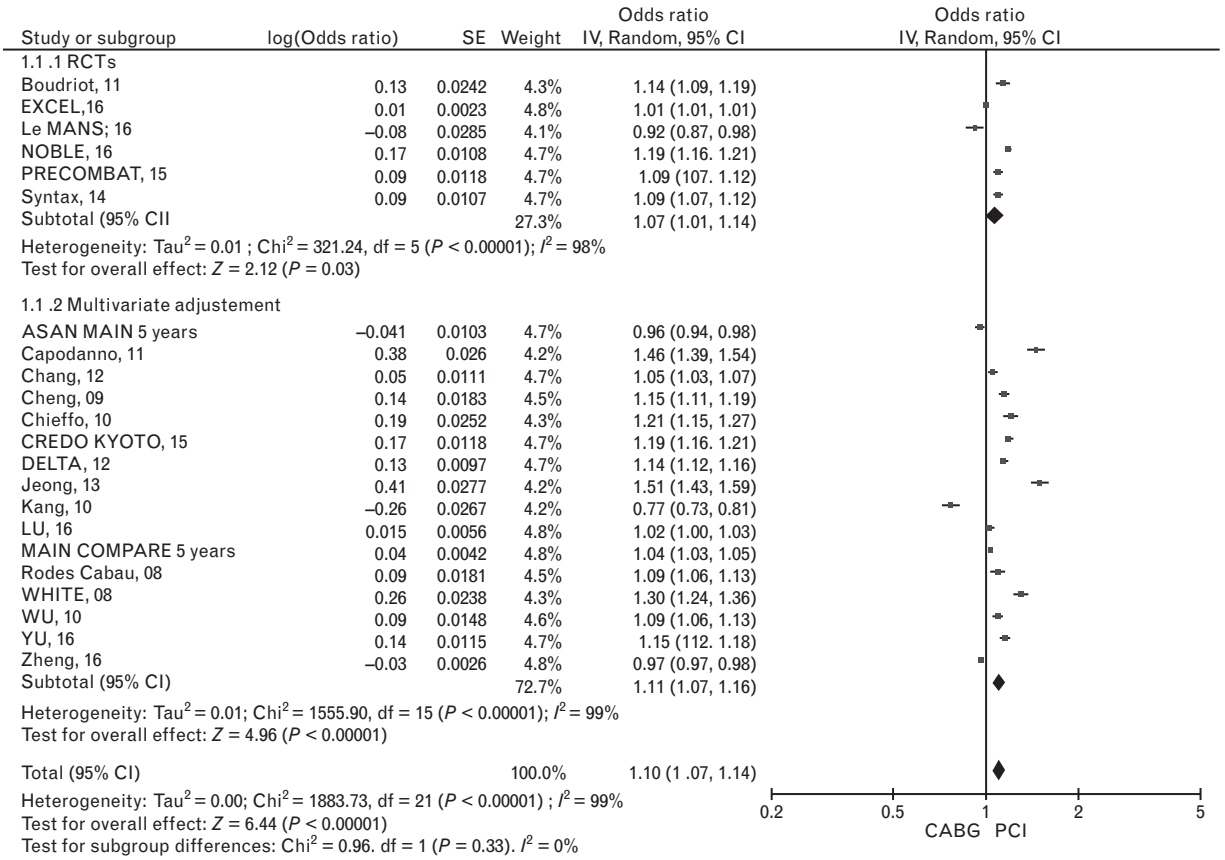
evaluated the incidence of MACEs in the two groups (8055 patients for PCI group and 10 037 for CABG group). After 5 (3–5.5) years, the overall incidence of events was higher in the PCI group compared with the CABG group (OR 1.10, 95% CI 1.07–1.14, $P < 0.01$). This result was confirmed in both NRCTs (OR 1.11; 95% CI 1.07–1.16, $P < 0.00001$), and RCTs subgroups (OR 1.07; 95% CI 1.01–1.14, $P = 0.03$; see Fig. 2 and S2 in web appendix, http://links.lww.com/JCM/A134) and considering only studies not including revascularization in the MACE definition (see Figure S1 in web appendix, http://links.lww.com/JCM/A134).

Secondary endpoint analysis

All the studies selected for the primary endpoint were also included in the analysis of death. According to death there was a not significant trend for higher incidence in the CABG group in the general analysis (OR 0.94; 95% CI 0.89–1.00, $P = 0.05$), with a neutral result in the subgroups (OR 0.92; 95% CI 0.78–1.07; $P = 0.27$; and OR 0.95; 95% CI 0.89–1.02; $P = 0.14$, respectively for RCTs and NRCTs; see Fig. 3, panel a)

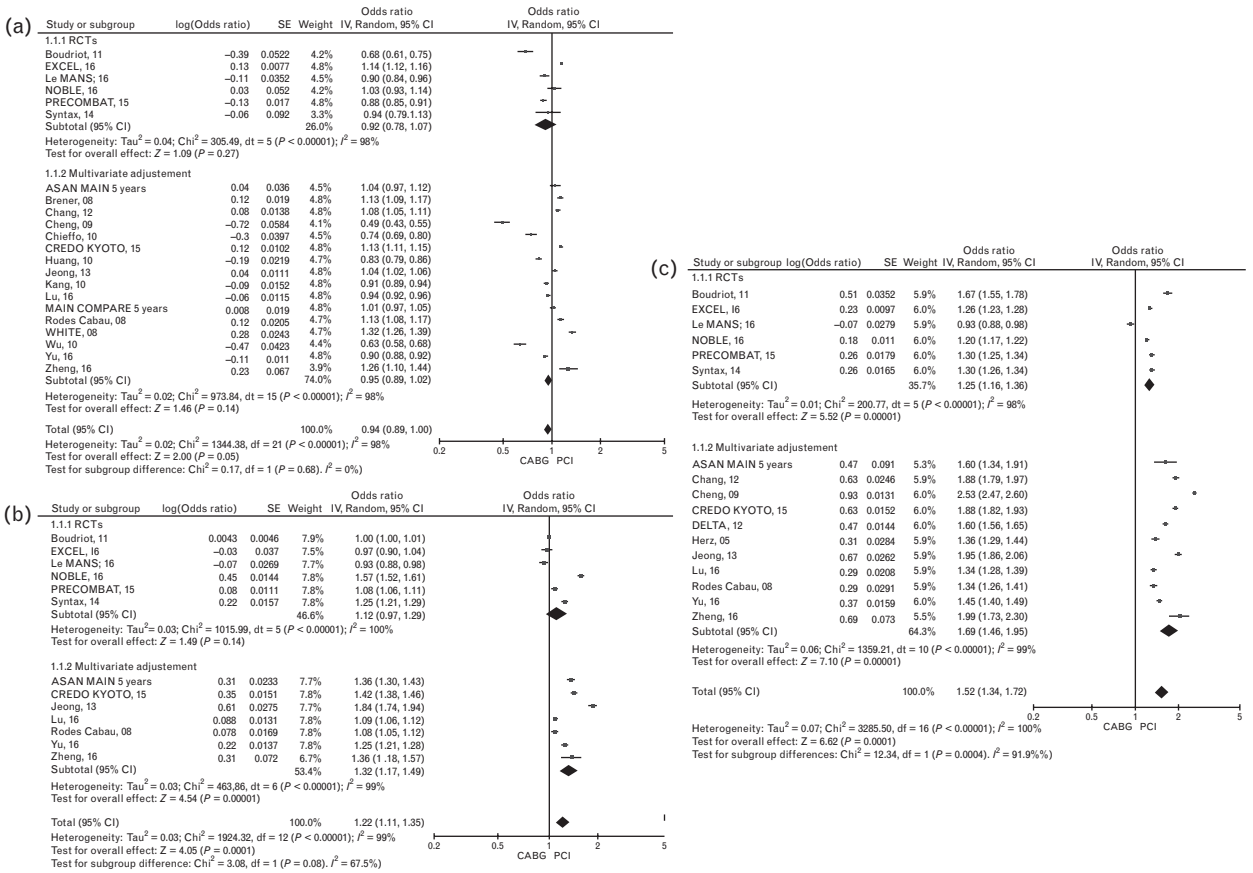
All RCTs and seven NRCTs (total patients 12 129, 7412 from NRCTs and 4717 from RCTs; 5278 for PCI, 8284 for CABG) evaluated incidence of MI. There was a significant higher incidence of MI in patients undergoing PCI compared with those re-vascularized by CABG (OR

Fig. 2



Incidence of MACEs. Major adverse cardiovascular events is meant in the present study as a composite of all-cause death, myocardial infarction, definite or probable stent thrombosis, and target vessel revascularization. In the upper part of the figure are shown results obtained from RCTs, in the middle results from multivariate adjusted clinical trials and in the lower part the combination of both. Global odds ratio for MACE: OR 1.10, 95% CI 1.07–1.14, *P* less than 0.01. Incidence of MACEs. MACE, major adverse cardiovascular events; OR, odds ratio; RCT, randomized controlled trial.

Fig. 3



(a–c) Incidence of death (a), myocardial infarction (b), and revascularization (c). Panel a: incidence of death. In the upper part of the figure are shown results obtained from RCTs, in the middle results from multivariate adjusted clinical trials and in the lower part the combination of both. Global odds ratio for death: OR 0.94; 95% CI 0.89–1.00, $P = 0.05$. Panel b: incidence of myocardial infarction. In the upper part of the figure are shown results obtained from RCTs, in the middle results from multivariate adjusted clinical trials and in the lower part the combination of both. Global odds ratio for MI: OR 1.22; 95% CI 1.11–1.35, P less than 0.00001. Panel c: incidence of revascularization. In the upper part of the figure are shown results obtained from RCTs, in the middle results from multivariate adjusted clinical trials and in the lower part the combination of both. Global odds ratio for revascularization: OR 1.52; 95% CI 1.34–1.72, P less than 0.00001. CI, confidence interval; OR, odds ratio; MI, myocardial infarction; RCT, randomized controlled trials.

1.22; 95% CI 1.11–1.35, $P < 0.00001$). This result was substantially determined by NRCTs (OR 1.32; 95% CI 1.17–1.49, $P < 0.00001$), whereas there was a nonsignificant trend favourable to CABG in RCTs (OR 1.12; 95% CI 0.97–1.29, $P = 0.14$; see Fig. 3, panel b) also excluding the NOBLE study (see Figure S2, web appendix, http://links.lww.com/JCM/A134).

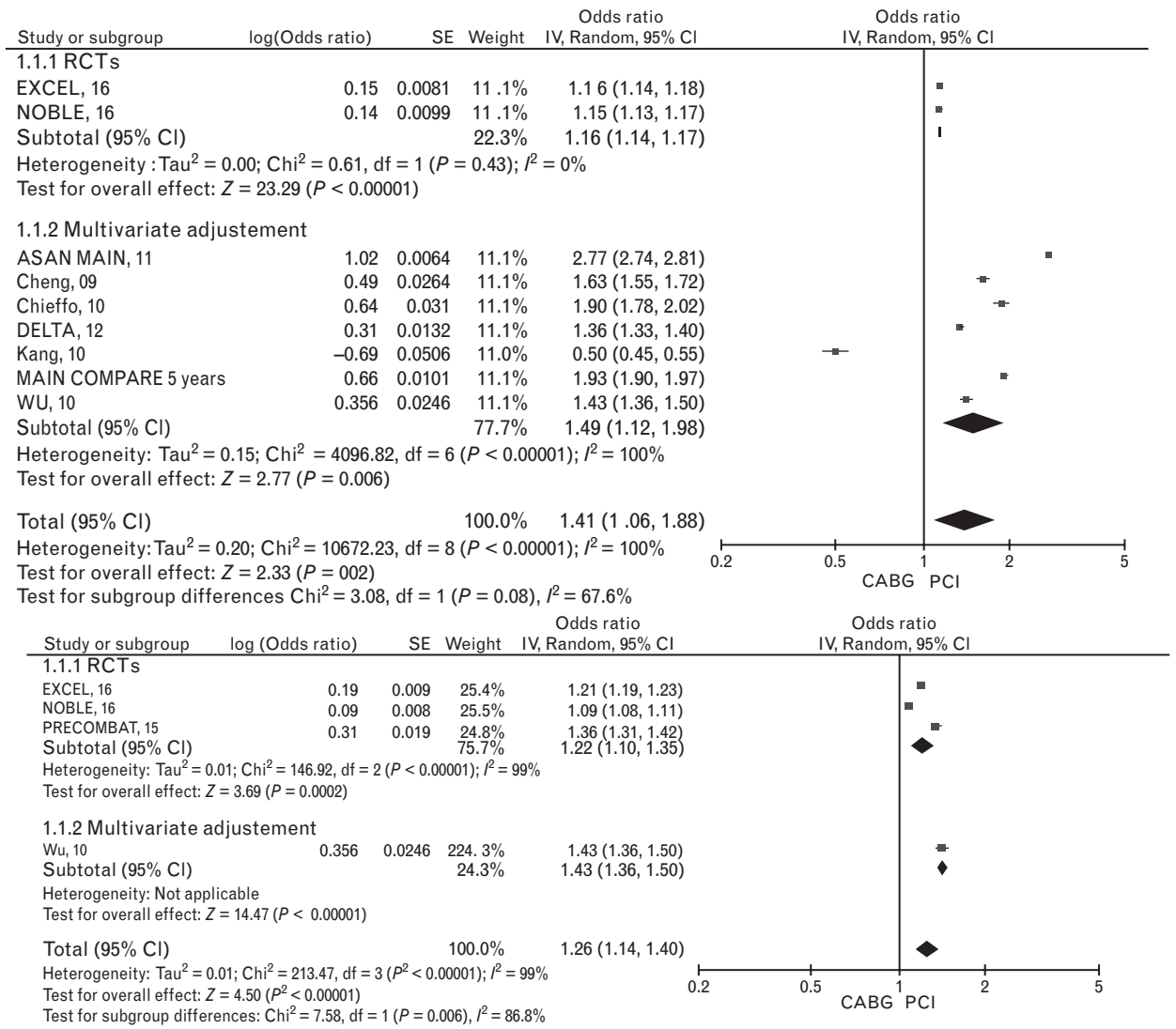
Seventeen studies (6 RCTs and 11 NRCTs, total patients 14 342, 4717 from RCTs and 9625 from NRCTS, 6509 for PCI, 7992 for CABG) were included for revascularization. The overall rate was significantly higher in the PCI group (OR 1.52; 95% CI 1.34–1.72; $P < 0.00001$) than in the CABG group (see Fig. 3c). This result was confirmed in both subgroups: OR 1.25; 95% CI 1.16–1.36 ($P < 0.01$) for RCTs and OR 1.69; 95% CI 1.46–1.95 ($P < 0.01$) for NRCTs. Similarly, PCI increased risk of TLR and ischemia-driven revascularization (see Fig. 4).

At meta-regression analysis, the use of two arterial graft or first generation drug eluting stents (DES) correlated with the higher incidence of repeated revascularization with PCI [beta 0.15 (0.12–0.18) and 0.2 (0.15–0.24)], respectively, for two arterial grafts and use of first generation DES. Distal left main resulted not significant [beta 0.08 (0.02–1.7), $P = 0.51$], whereas use of intravascular ultrasound (IVUS) was protective [beta −0.02 (−0.09 to −0.01); see Fig. 5a–c].

Regarding in-hospital events, from the analysis of 10 studies (of which two were RCTs), PCI reduced risk of death (OR 0.70; 95% CI 0.57–0.86, $P < 0.01$), as well as stroke (OR 0.59; 95% CI 0.38–0.93; $P = 0.02$; see Figure S4, web appendix, http://links.lww.com/JCM/A134).

Finally, 12 studies (four RCTS) reported the incidence of stent thrombosis (total patients 6542, 2208 from RCTs and 4334 from NRCTs) whereas 6 (3 RCTs) described

Fig. 4



Incidence of target lesion revascularization (above) and ischemia-driven target lesion revascularization (below). Global OR for TLR: 1.41; 95% CI 1.06–1.88, *P* less than 0.02. Global OR for ischemia-driven TLR: 1.26; 95% CI 1.14–1.40, *P* less than 0.00001. CI, confidence interval; OR, odds ratio; TLR, target lesion revascularization.

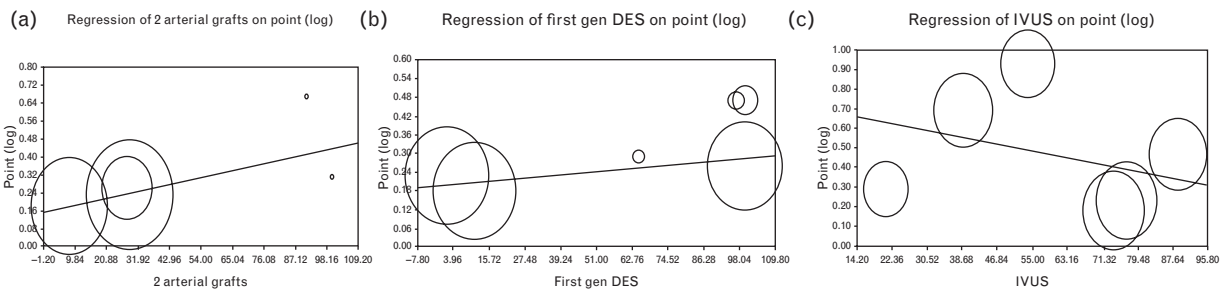
rate of graft occlusion (3007 total patients, 1903 from RCTs, 1104 NRCTs). The analysis of these data showed a higher incidence of graft occlusion compared with definite or probable stent thrombosis, respectively, 3.24% (2.25–4.23) for graft occlusion and 2.13% (1.28–2.98) for stent thrombosis (see Fig. 6a and b). Specific outcomes definition and data on a single-study basis are described in supplementary appendix (see Tables S5-S7, web appendix, http://links.lww.com/JCM/A134).

Subgroup analysis for Syntax score

Five studies evaluated (two RCTs and three NRCTs, 2886 patients in PCI group, 4398 in CABG group) MACEs in patients with a Syntax score less than 22 showing similar outcomes between the two strategies (OR 1.15; 95% CI 0.98–1.35, $P=0.08$).

Two thousand five hundred and thirty-three patients, 1087 in the PCI group and 1446 in the CABG group, with an intermediate Syntax score (22–32) were analysed in three studies (two RCTs). MACE rate was higher in the PCI group (OR 1.26; 95% CI 1.05–1.5; $P=0.01$). An analogue result was obtained for patients with a Syntax score > 32, from a meta-analysis of two RCTs and two NRCTs including this high-risk population (total patients 6956; PCI 2766, CABG 4190) (OR 1.27: 1.19–1.36; $P<0.0001$). All these results did not change removing NRCTs from the analysis.

Fig. 5



Meta-regression of two arterial grafts on revascularization (a); meta-regression of first generation DES on revascularization (b); meta-regression of IVUS on revascularization (c). Panel a: correlation between the use of two arterial graft and the incidence of revascularization, beta 0.15 (0.12–0.18). Panel b: correlation between the use of first generation DES and the incidence of revascularization, beta 0.2 (0.15–0.24). Panel c: benefit of IVUS use on incidence revascularization, beta −0.02 (−0.09 to −0.01).

Three studies (of which two were RCTs) reported the incidence of death among patients with a Syntax score less than 22. There was a nonsignificant higher incidence of all-cause death in patients treated with PCI (OR 1.43; 95% CI 0.82–2.51, $P = 0.21$). Only one RCT was available for intermediate Syntax score (22–32), with higher risk for PCI (OR 1.28; 95% CI 1.21–1.36, $P < 0.00001$).

Three articles (two RCTs) were included for high-risk patients (Syntax >32) without difference (OR 1.04; 95% CI 0.43–2.52, $P = 0.92$). For this subgroup, the exclusion of NRCTs from the analysis did not significantly change the result.

A subgroup analysis for Syntax score was also performed for revascularization. Three trials (two RCTs involving 5351 patients, 2099 for PCI and 3252 for CABG) reported this endpoint for patients with Syntax score less than 22, resulting in a nonsignificant higher incidence of revascularization for the PCI group (OR 1.43; 95% CI 0.82–2.51, $P = 0.21$). Result reached statistical significance after excluding NRCT (OR 1.11; 95% CI 1.08–1.14). More repeated revascularizations were also observed in patients with intermediate Syntax score (OR 1.28; 95% CI 1.21–1.36, $P < 0.00001$). One RCT was available as well with Syntax score greater than 32 (OR 1.71; 95% CI 1.55–1.89, $P < 0.0001$, from two RCTs and one NRCT, see figures S5, web appendix, http://links.lww.com/JCM/A134).

Discussion

To the best of our knowledge, this is the first meta-analysis including data from all RCTs comparing PCI versus CABG for ULMCA, along with data from observational studies with multivariate adjustment.

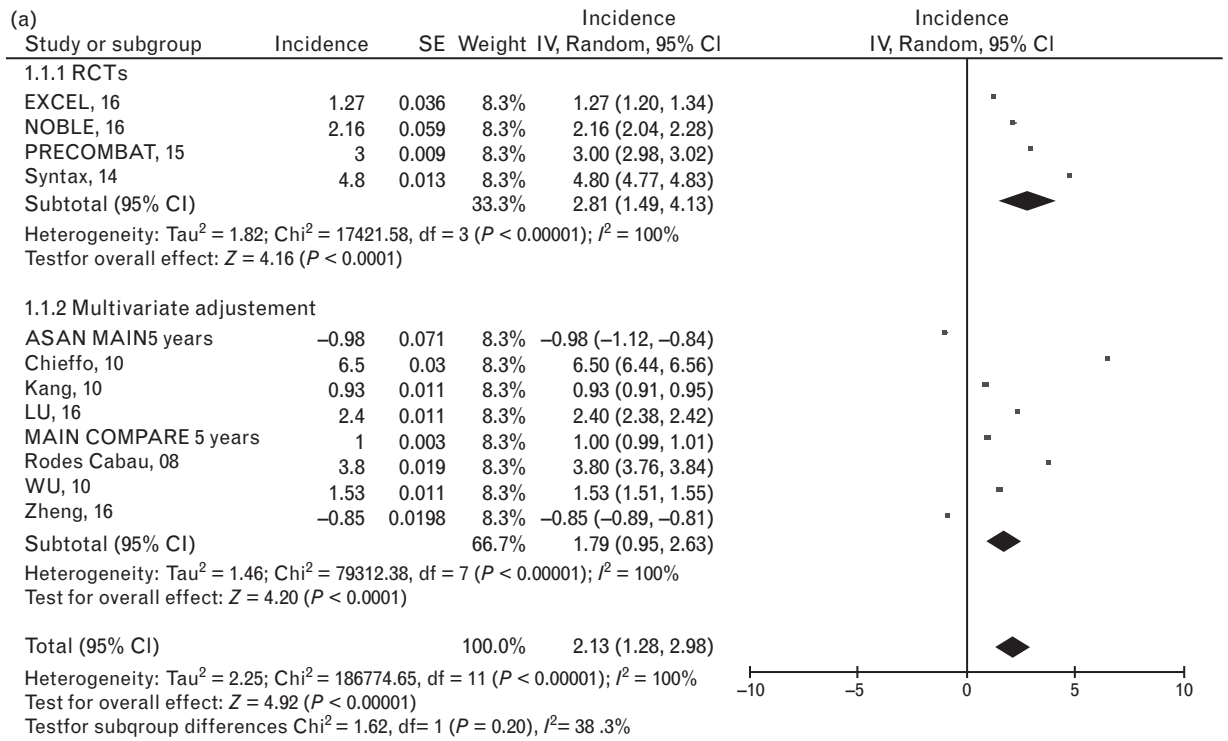
The main results were:

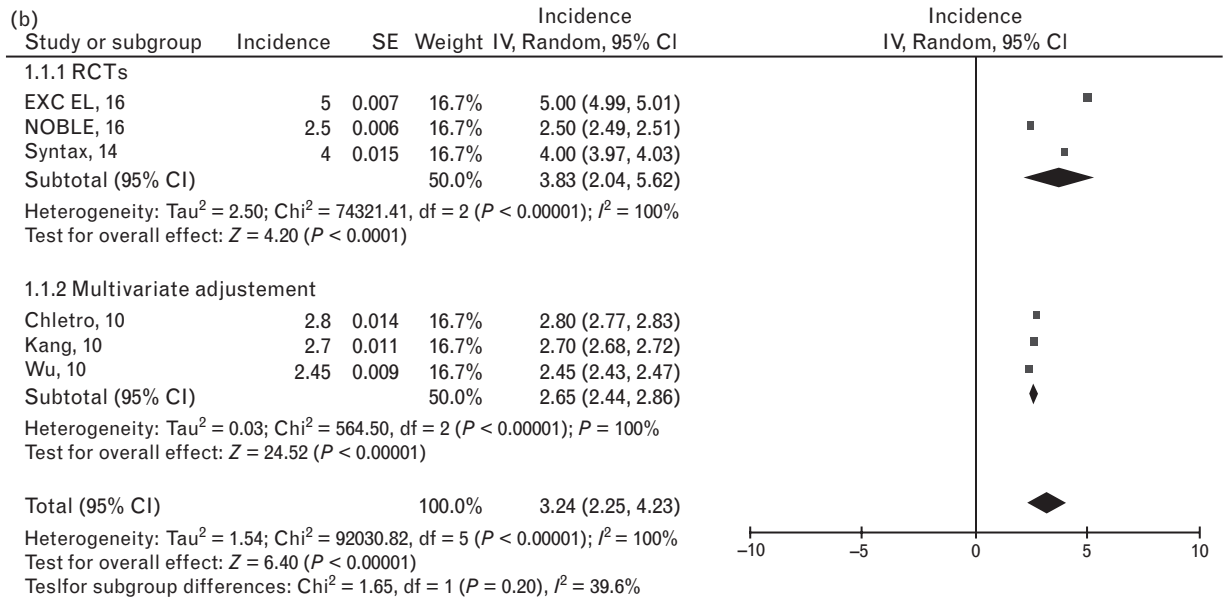
(1) At a mean follow-up of 5 years, there were more MACEs with PCI strategy than CABG; this result is mainly driven by a higher incidence of repeated revascularization particularly in case of complex lesions (Syntax score ≥22);
(2) The difference in terms of repeated revascularization was more evident using first generation DES and for patients treated with two arterial conduits, whereas use of IVUS improved performance of PCI;
(3) Stroke incidence and hospital death were higher with CABG strategy.

At a medium- to long-term follow-up, patients who underwent ULMCA revascularization with PCI showed a slightly higher (10% increase) incidence of MACE. Even if MACE represented a widespread used composite endpoint in the scientific community, thanks to its ability to reduce the sample size needed by researchers, its heterogeneous definition generated important divergences in result interpretation.[16] For example, the two recently published RCTs on this theme, the NOBLE and EXCEL trials,[2,6] showed apparent discordance in terms of primary composite outcome that can probably be justified by the inclusion of revascularization in the first and the exclusion in the second one. Focusing on single component outcome, our meta-analysis highlighted that although no significant differences emerged in terms of overall mortality, revascularizations were more frequent with PCI strategy both in randomized and in nonrandomized studies, whereas reduction of MI offered by CABG was evident only after adding observational studies. These results were substantially consistent with all previously published studies and meta-analysis[2,5] even if only Athappan *et al.*[17] evidenced a trend for more MI with PCI.

Correlation between lesion complexity and outcome has been confirmed by the present analysis. In the Syntax score subanalysis, the statistical significance for the need for new revascularization at follow-up was achieved for Syntax score ≥22 with a subsequent clear

Fig. 6





Incidence of stent thrombosis (a) and graft occlusion (b). Panel a: incidence of stent thrombosis. In the upper part of the figure are shown results obtained from RCTs, in the middle, results from multivariate adjusted clinical trials and in the lower part, the combination of both. Global odds ratio for stent thrombosis. Panel b: incidence of graft occlusion. In the upper part of the figure are shown results obtained from RCTs, in the middle results from multivariate adjusted clinical trials and in the lower part the combination of both. RCT, randomized controlled trials.

linear correlation for incremental values. This report was well known since Syntax score publication[18] and clearly implemented in European and American guidelines indication.[19,20] Similarly, our data demonstrated that in patients with low Syntax score, rates of revascularization did not differ among PCI and CABG, whereas risk of death did not differ across the subgroups.

Specific revascularization techniques influenced the risk of subsequent revascularization. According to our meta-regression analysis, the higher incidence of revascularization in PCI patients was more evident with the use of first generation DESs and when compared with those treated with two arterial grafts, whereas it was reduced by the use of IVUS. The majority of studies considered in our meta-analysis used first generation DES. Last generation DESs, with their more biocompatible structure, have been shown to have the potentiality to decrease incidence of repeated revascularizations, stent thrombosis and consequently MACEs in head-to-head comparison versus previous generation, even if mainly in other lesion settings[8,21,22] with little evidence on left main treatment[23–26] and in terms of PCI versus CABG comparison.[2,6] The NOBLE and EXCEL trials compared Biolimus-eluted stent (BES) and fluoro-polymer-based cobalt–chromium everolimus-eluting stents (EES), respectively, to CABG strategy. At a mean follow-up of 5 and 3 years, patients in PCI cohorts needed more repeated revascularization and experience more nonprocedural MI. Of note, a significant difference emerged only for total revascularization, whereas TLR were similar between the two groups. These findings confirmed a good outcome of PCI with new DESs on left main lesions, whereas the repeated revascularizations were probably because of CAD progression in other sites. More data with the use of new DESs are needed to better clarify these results. Moreover, benefit of use of IVUS is largely known with DES,[4,27] as a means to optimize procedural performance, resulting in improved long-term clinical outcomes. On the other hand, the use of multiple arterial grafting seemed to increase CABG benefit in our analysis. This result is consistent with a very large amount of observational evidence.[28] However, the recently published interim 5-year analysis of the ART trial[7] did not find any survival benefit with the use of bilateral mammary artery graft with a concomitant increase in wound complications. The lack of power to detect significant differences in hard outcomes at 5 years' follow-up, the high rate of cross-over between groups, the use of the radial artery in almost 30% of the patients in the single mammary group and the exceptionally high compliance with optimal medical therapy can probably explain the negative results of this article. It is reasonable to suppose that multiple arterial grafting, whenever technically feasible and especially in younger patients, could give a long-term benefit compared with venous bypass and single internal mammary artery and to PCI as suggested by our meta-analysis.

The higher incidence of stroke in CABG patients stressed the importance of a tailored approach for the choice between percutaneous and surgical revascularization. The present result confirmed those previously evidenced by several meta-analyses[17,29] and can probably be linked to the higher in-hospital mortality with CABG that emerged in our study. Consequently, whenever evaluating a patient with ULMD, the risk of in-hospital complication according to single-patient risk should be carefully weighed against that of subsequent revascularization, also according to Syntax score.

Limitation

Our study presents many limitations. As results were analysed on an aggregate data basis, no assessment of between-group equal distribution of baseline characteristics was possible. As with any meta-analysis, all included studies' limitations are shared by our work; the statistical heterogeneity among the studies included in the primary and secondary outcomes' analysis resulted as always severe, whereas for publication bias funnel plot analysis showed that it was not relevant, as confirmed by nonsignificant Egger's test ($P = 0.57$; see appendix, Figure S1, http://links.lww.com/JCM/A134). Finally, some results show borderline statistical significance so that a larger sample size as well as a longer follow-up could increase statistical reliability for the present results.

Conclusion

CABG reduced risk of repeated revascularization compared with PCI in patients with ULMCA, especially for those with Syntax score more than 22, with a higher risk of in-hospital death. Use of double arterial grafts improved performance of CABG as well as intra-coronary imaging did for PCI approach.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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